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(54) ANTIMICROBIAL PEPTIDE ORIGINATING FROM PANDINUS IMPERATOR

(57)Abstract:

PROBLEM TO BE SOLVED: To provide a new peptide that is isolated from the venom extracted from Pandinus impertor, a kind of scorpion.

SOLUTION: One of the isolated peptides is represented by the following amino acid sequence: Gly Lys Val Trp Asp Trp Ile Lys Ser Ala Ala Lys Lys Ile Trp Ser Ser Glu Pro Val Ser Gln Leu Lys Gly Gln Val Leu Asn Ala Ala Lys Asn Tyr Val Ala Glu Lys Ile Gly Ala Thr Pro Thr; and the other peptide is represented by the following amino acid sequence: Phe Trp Gly Ala Leu Ala Lys Gly Ala Leu Lys Leu Ile Pro Ser Leu Phe Ser Ser Phe Ser Lys Lys Asp; or the C-terminus of the peptide is amidated. These peptides have antibacterial activity and is useful as an antibacterial.

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CLAIMS

[Claim(s)]

[Claim 1] The antibacterial peptide of the scorpion venom origin.

[Claim 2] This peptide is pan DINUSU. Antibacterial peptide according to claim 1 isolated from the venom of in PERETA (Pandinus imperator).

[Claim 3] The antibacterial peptide according to claim 1 or 2 this whose peptide is a peptide expressed with following amino acid sequence type:Gly Lys Val Trp Asp Trp Ile Lys Ser AlaAla Lys Lys Ile Trp Ser Ser Glu Pro ValSer Gln Leu Lys Gly Gln Val Leu Asn AlaAla Lys As.

[Claim 4] This peptide is the following amino acid sequence type :P The peptide expressed with he Trp Gly Ala Leu Ala Lys Gly Ala LeuLys Leu Ile Pro Ser Leu Phe Ser Ser PheSer Lys Lys Asp, or antibacterial peptide according to claim 1 or 2 which is a peptide with which the C-end was amidated.

[Claim 5] Drugs which contain the peptide of a publication as an active principle in claim 1 thru/or any 1 term of 4.

[Claim 6] Use as an antimicrobial agent of a peptide given in claim 1 thru/or any 1 term of 4.

[Claim 7] The antimicrobial agent which consists of an effective dose of the antibacterial peptide of the scorpion venom origin as an active principle, and support permitted in medicine manufacture.

[Claim 8] This peptide is pan DINUSU. Antimicrobial agent according to claim 7 isolated from the venom of in PERETA (Pandinus imperator).

[Claim 9] This peptide The following amino acid sequence type : Gly Lys Val Trp Asp Trp Ile Lys Ser AlaAla Lys Lys Ile Trp Ser Ser Glu Pro ValSer Gln Leu Lys Gly The antimicrobial agent according to claim 7 or 8 which is the peptide expressed with Gln Val Leu Asn AlaAla Lys Asn Tyr Val Ala Glu Lys Ile GlyAla Thr Pro Thr.

[Claim 10] This peptide is the following amino acid sequence type :P Antimicrobial agent according to claim 7 or 8 which is the peptide expressed with he Trp Gly Ala Leu Ala Lys Gly Ala LeuLys Leu Ile Pro Ser Leu Phe Ser Ser PheSer Lys Lys Asp, or the peptide with which the C-end was amidated.

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DETAILED DESCRIPTION

[Detailed Description of the Invention]

[0001]

[Field of the Invention] This invention is pan DINUSU which is a kind of a scorpion. It is related with the new antibacterial peptide of the poison origin of in PERETA (Pandinus imperator).

[0002]

[Description of the Prior Art] a scorpion -- the venom of a kind and Araneida serves as a resource with abundant bioactive components, and peptides are compounds important for effective medicinal research and development to a vertebrate and an insect also in it. According to some researches, it is shown clearly that the effective poison component of new peptide nature is contained in the venom of Araneida to bacteria or an eukaryotic cell.

[0003] Recently, the crude venom (380 S. Haeberli et al., Toxicon, 38:373- 2000) of Cupiennius salei which is a kind of the poison spider to the antibacterial peptide was isolated from the crude venom (2066 Yan and Adams, J.Biol.Chem., 273:2059- 1998) of Lycosa sp. which is a kind of the poison spider. Moreover, Androctonus australis (29544 L. Ehret-Sabatier et al., J.Biol.Chem., 271:29537- 1996) to the antibacterial peptide is isolated from Lieurusquinquestriatus hebraeus (22 S. Cociancich et al., Biochem.Biophys.Res.Comm., 194:17- 1993) which is a kind of a scorpion. However, these antibacterial peptides are isolated from the hemolymph liquid of a scorpion.

[0004] furthermore, the skin (M. -- Zasloff, Proc.Natl.Acad.Sci., USA, 84:5449-5453, 1987; J.M.Park et al. --) of the frog of a Rana kind Biochem.Biophys.Res.Comm., 205:948-954, 1994; N.Morikawa et al., Biochem.Biophys.Res.Comm. and 189:184- from 190 and 1992 And some peptides which have the same antimicrobial activity and lysis activity are isolated from the hemolymph liquid (16 D. Hultmark, Eur.J.Biochem., 106:7- 1980) of a moth.

[0005] And the patent is already given about the application [as opposed to / some / of these peptides / a pathogenic cell] (for example, U.S. patent No. 5,686,563; 5,889,148; 5,912,231; 5,962,410).

[0006] therefore, a scorpion -- although it was important to isolate the new antibacterial peptide which has the operation over a pathogenic cell from the venom of a kind, the attempt which still isolates such a peptide was not made.

[0007]

[Problem(s) to be Solved by the Invention] In view of the above-mentioned present condition, this invention makes it a technical problem to isolate an antibacterial peptide newer than the venom of a scorpion, and to apply to physic.

[0008]

[Means for Solving the Problem] It is pan DINUSU whose this invention persons are kinds of a scorpion in order to solve this technical problem. While isolating the antibacterial peptide newer than the crude venom of in PERETA (Pandinus imperator) and clarifying the chemical description, it inquired wholeheartedly about the bioactive. consequently, as two new peptides which have antimicrobial activity and hemolysis activity The peptide shown by the array number 1 (this is named pan date KISHIN 1) The peptide hereafter shown by the array number 2 and it may indicate it as Pim1 (this is

named pan date KISHIN 2) the case where it is hereafter indicated as Pim2 -- it is -- it isolates, and this thing checked that it was effective to the pathogenic bacteria and cell of Homo sapiens and an animal, and completed this invention.

[0009] Therefore, this invention is pan DINUSU. The new antibacterial peptide obtained from the venom of in PERETA (Pandinus imperator) is offered.

[0010] This invention offers the antibacterial peptide (pandate KISHIN 1 (Panditoxin 1) ;P [1] im.) expressed with the following amino acid sequence type: Gly Lys Val Trp Asp Trp Ile Lys Ser AlaAla Lys Lys Ile Trp Ser Ser Glu Pro ValSer Gln Leu Lys Gly Gln Val Leu Asn AlaAla Lys Asas the concrete mode.

[0011] This invention is the following amino acid sequence types as still more nearly another concrete mode :P The antibacterial peptide (pandate KISHIN 2 (Panditoxin 2) ;P [2] im.) expressed with he Trp Gly Ala Leu Ala Lys Gly Ala LeuLys Leu Ile Pro Ser Leu Phe Ser Ser PheSer Lys Lys Asp or the peptide with which the C-end was amidated is offered.

[0012]

[Embodiment of the Invention] The antibacterial peptide which this invention offers is pan DINUSU which is a kind of a scorpion. After 0.1% trifluoroacetic acid (it abbreviates to TFA hereafter) content water solution containing about 10% of acetonitrile extracting the venom of in PERETA (P. imperator) and obtaining a crude extract, subsequently to conventional methods, such as reversed phase chromatography or ion exchange chromatography, the target peptide can be obtained by following and refining [isolate and] this crude extract.

[0013] Consequently, this invention persons succeeded in obtaining two kinds of following antibacterial peptides.

[0014] Pan date KISHIN 1 (Pim1) [Panditoxin 1]

Gly Lys Val Trp Asp Trp Ile Lys Ser AlaAla Lys Lys Ile Trp Ser Ser Glu Pro ValSer Gln Leu Lys Gly Gln Val Leu Asn AlaAla Lys As[0015] Pan date KISHIN 2 (Pim2) [Panditoxin 2]

Phe Trp Gly Ala Leu Ala Lys Gly Ala LeuLys Leu Ile Pro Ser Leu Phe Ser Ser PheSer Lys Lys Asp

[0016] Pan date KISHIN 1 indicated high homology (homology) to be DERUMASEPUCHIN (Dermaseptin) isolated from SEKUROPIN (Cecropin) isolated from Hyalophora cecropia which is a kind of a moth, and Phyllomedusa sauvagii which is a kind of a frog, as shown in the amino acid sequence type of the following table 1.

[0017] Moreover, pan date KISHIN 2 is the antibacterial peptide isolated from the skin of Rana rugosa which is a kind of a frog. GAEGURIN -5 (Gaegurin-5) (954 J. M.Park [et al.], Biochem.Biophys.Res.Comm., 205:948- 1994), and BUREBININ -1 (Brevinin-1) (N. -- Morikawa et al. --) which is the antibacterial peptide isolated from Rana brevipoda porsa which is a kind of a frog Biochem.Biophys.Res.Comm. and 189:184- high homology (homology) was indicated to be 190 and 1992.

[0018]

[Table 1] Table 1: Sequence Alignment (Sequence alignment)

ペプチド	配列	Pim 1 との 相 同 性 (%)
Panditoxin 1	GKVWDWIKSAAK--	—
Esculentin	KIWSSEPVSQ LK GQVLNAAKNYVAEKIGATPT	57.6
Cecropin	GIFSKLGRKKIKNLLISGLKNVGKEVGMDVVRTGIDI	59.7
Dermaseptin	AGCKIKGEC --KWKLFKKIEK--VGQNIRDGIIKAGPAVAVVG-- QATQIAK--- -ALWKTMLKKLG---TMALHAGKAALGAAADTIS-- QGTQ-----	55.2
		Pim 2 との 相 同 性 (%)
Panditoxin 2	FWGALAKGALKLIPSLFSSFSKKD	—
Brevinin 1	FLPVLAGIAAKVVPALFCKITKKC	75.2
Gaegurin 5	FLGALFKVASKVLPSVKCAITKKC	73.2
Gaegurin 6	FLPLLAGLAANFLPTIICKISYKC	65.4
Pipinin 1	FLPIIAGVAAKVFPKIFCAISKKC	72.2
Pipinin 2	FLPIIAGIAAKVFPKIFCAISKKC	71.4
Pipinin 3	FLPIIASVAAKVFSKIFCAISKKC	72.0
Magainin 1	GIGKFLHSAGKFGKAFVGEIMKS-	60.4
Magainin 2	GIGKFLHSAKKFGKAFVGEIMNS-	59.7

[0019] Sequence Clustalx performed alignment (Sequence alignment) using the Pulse-Amplitude-Modulation250 protein weight matrix by the PromSED program. In addition, the sequence of an array is corrected after alignment for analysis. The homology of an array expressed the rate to Pim1 and Pim2 with the percentage based on the result of Pulse Amplitude Modulation250. Moreover, the gap in array expression (it displays by "-") was inserted in order to give approximation nature to array expression.

[0020] the peptide which this invention offers -- setting -- some amino acid -- deletion, addition, and a permutation -- they are included by the technical range of the peptide of this invention as long as the same pharmacological activity as the natural peptide of this invention is shown, even if the C-end is amidated further. Such a peptide is also included again all over the technical range of this invention relevant to the use as an antimicrobial agent.

[0021]